REMARKS:

Claim 5 has been amended to emphasize the multiplex nature of the invention. Support for this amendment may be found throughout the application as filed, for example at least at page 6, line 32 to page 7, line 6 and page 10, line 6 to page 12, line 5 and page 20, lines 20-23. The reference to '15 or more continuous nucleotides' has also been deleted.

Claim 5 was rejected under 35 USC 102(b) as anticipated by Pass et al.

Claim 5 was rejected under 35 USC 102(b) as anticipated by Gannon et al.

Specifically, in both cases, the office action states that the claimed primers are 'inherent in the genes and primers' taught by the prior art.

Applicants respectfully request that the examiner reconsider these rejections. Specifically, the primers described above have been selected based on their ability to give clean and consistent results when used with other primer pairs within the multiplex system. As discussed above, claim 5 has been amended to incorporate the multiplex aspect of the invention, specifically, the ability to combine the primers of claim 5 with primers used for the amplification of other virulence genes.

Specifically, the primers described in the instant application can be used to detect stx1, stx2, stx2c, stc2d, stx2e, stx2f, eaeA, EHEC hlyA, rfbeO157, flicH7 and 16s rRNA by multiplex PCR as discussed in the application as filed and in claim 5. The primers are very specific for the detection of these genes

without the use of restriction enzymes. The use of other primer combinations aside from the VT1 and VT2 primer pairs described in claim 5 with the other primers may lead to non-specific PCR cross reactions when used in a multiplex assay, rendering the assay useless and non-informative. Accordingly, applicants believe that the VT-1 and VT-2 primers described by Pass et al. and Ganon et al. as multiplex primers can not be used in place of the primers described in the instant application, that is, cannot be used in combination with the disclosed primer pairs for the detection of at least one of the following *Escherichia coli* virulence-related genes selected from the group consisting of: eaeA, EHEC-HlyA, Stx2c, Stx2d, Stx2e, rfbE and flic.

Applicants respectfully note that many primers detecting VT-1 and VT-2 have been published since the late 1980s or early 1990s. However, these primers can not just be simply integrated into a multiplex system due to a variety of unpredictable factors including but by no means limited to primer-dimer formations, primer-sequence secondary structure anomalies, PCR reaction conditions, primer-primer interference phenomena, PCR amplicon size variations and other problematic issues which may result in the product being unreliable, unpredictable or irreproducible. In essence, PCR reactions often produce unexpected and/or unexplainable results and the selection of primers for use in a multiplex system such as described in the instant application and amended claims is not always straight-forward and accordingly applicants maintain that the selection of such primers cannot be 'inherent'.

Applicants further note that one primer pair is derived from the B-subunit and is highly specific for VT-2. In contrast, for example, those of Pass et al. are derived from the A-subunit and will cross react with other VT-2 subtypes and therefore cannot identify each separately without multiple digestions and PCR steps. In this respect the primers taught by Pass cannot both detect and separate the different virulent subtypes of this pathogen. To achieve this, a further step and additional primers would need to be used.

In view of the foregoing, further and more favorable consideration is respectfully requested.

Please charge the additional amount of $340 to our deposit account 01-0310. A fee for the one month extension of time has already been charged.

Respectfully submitted

Gehua Wang et al.

PER: _____
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MRW/
August 8, 2008
Enc.()

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